RESEARCH PROCESS

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Clinical Trials Study

RANK-ligand and osteoprotegerin as biomarkers in the differentiation between periprosthetic joint infection and aseptic prosthesis loosening

The role of the RANKL/RANK/OPG system has not yet been examined in the differentiation between PJI and aseptic prosthesis loosening. In this study we therefore defined the sensitivity, specificity and accuracy of RANKL and OPG in patients with PJI versus aseptic loosening and compared these results to current standards of diagnostic testing. Patients with total joint replacement without signs of PJI or aseptic loosening served as control group. Furthermore, we tested whether there is a difference between loosened and stable implants in the serum levels of these and other parameters. Our hypothesis was that the measured serum levels of RANKL and OPG correlate positively (1) with the presence of PJI and 2) with implant loosening. Secondly we investigated if the serum levels of calcium, phosphate and alkaline phosphatase would be different in stable or loosened implants. 120 patients presenting with a painful total knee or hip arthroplasty with indication for surgical revision were included in this prospective clinical trial. Preoperative serum samples were collected and analyzed for RANKL, OPG, calcium, phosphate, AP and the bone-specific subform of AP. The definite diagnosis of periprosthetic joint infection was determined on the basis of established clinical, serological, microbiological and histopathological examination. White blood cell count (WBC) was determined from the blood samples, and serum samples were analyzed for C-reactive protein (CRP) (Dimension Vista, Siemens Medical Solutions Diagnostics GmbH, Eschborn, Germany), RANKL and OPG (Sandwich ELISA, Fa. BioVendor GmbH, Heidelberg, Germany); Serum calcium (Ca), serum phosphate

(PO_4), alkaline phosphatase (AP) and the bone-specific subform of the AP (bAP) were also analyzed in serum (Immunolite, Siemens, Eschborn, Germany). Ratio of RANKL/OPG was calculated from the determined values. Intraoperatively, tissue specimens were taken for microbiological and histological analysis, the intraoperative aspect was recorded, as well as the surgeons' statement whether the implant was stable or loose. Data were collected in Microsoft Excel (Microsoft Corporation, Richmond, USA), and statistical analysis was carried out using GraphPad Prism 5.04 (GraphPad Software, La Jolla, CA, USA), testing for statistical significance between the three groups with Kruskal-Wallis-ANOVA without assuming normal distribution and with Dunn's post-hoc test. According to the results, we had to discard our above mentioned hypotheses, as we found no significant differences in the mean values of circulating RANKL and OPG in PJI vs. AL or control group, but with a certain trend of lower RANKL concentrations and higher OPG concentrations in the PJI group. A RANKL/OPG ratio > 60 ruled out PJI in all cases (Specificity: 100%, 95% CI: 89,11% to 100,0%). In the differentiation between stable and loose implants, none of the parameters assessed showed a significant difference which let to the conclusion that the sole use of these parameters for differentiating PJI and aseptic loosening cannot be recommended, but they may have utility as a conformation test.